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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/320,156	05/26/1999	MICHAEL ROSENBLUM	D5425CIP2	4227

7590 06/14/2006

David L Parker  
FULBRIGHT & JAWORSKI LLP  
600 Congress Avenue Suite 2400  
Austin, TX 78701

EXAMINER
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CANELLA, KAREN A

ART UNIT	PAPER NUMBER
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1643

DATE MAILED: 06/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/320,156

Applicant(s)

ROSENBLUM ET AL

Examiner

Karen A. Canella

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☐ Claim(s) 1-17 and 19 is/are pending in the application.  
4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☐ Claim(s) 1-17 and 18 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_.

### **DETAILED ACTION**

The finality of the Office action, mailed May 23, 2002 is withdrawn in light of the rejections below.

The amendment filed May 8, 2003 has been entered. Claim 18 has been canceled. Claim 15 has been amended. Claims 1-14, 20 and 21 remain withdrawn from consideration. Claims 15-17 and 19 are under consideration.

Acknowledgment is made of applicants claim to an earlier effective filing date via 08/404,499, filed 3/17/1995; 08/300,082, filed 9/2/1994. Upon review of 08/300,082, it is noted that the disclosure lacks adequate support for the scFv-23 single chain antibody on which all of the instant claims depend. The first mention of the svFv-23 antibody appears in the 08/404,499 application. One of skill in the art would reasonable conclude that applicant was not in possession of the svFv-23 antibody conjugate before 3/17/1995, therefore the earliest effective filing date for the instant invention will be 3/17/1995.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 15 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over King et al (U.S. 5,587,458) in view of Rosenblum et al (Cancer Communications, 1991, Vol. 3, pp. 21-27, cited in a previous Office action).

King et al teach conjugates of the single chain antibody, e23 (column 6, lines 58-62), which appears to be identical to the instant scFv23. King et al teach conjugation of anti-ERbB2 antibodies with anti-tumor drugs, toxins or radionuclide (column 4, lines 9-15). King et al do not specifically teach conjugation of e23 to TNF (column 8, lines 47-67).

Rosenblum et al teach that the sensitivity of tumor cells to TNF was dramatically augmented by antibody-mediated delivery to said cells.

It would have been prima facie obvious at the time the claimed invention was made to substitute TNF for the cytotoxic moiety in the e23 conjugates taught by King et al. One of skill

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in the art would have been motivated to do so by the teachings of Rosenblum et al pointing out the benefit of antibody-mediated delivery of TNF to tumor cells relative to the administration of free TNF.

Claims 15-17 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over King et al (U.S. 5,587,458) and Rosenblum et al (Cancer Communications, 1991, Vol. 3, pp. 21-27) as applied to claims 15 and 19 above, and further in view of Gillies (U.S. 5,650,150).

Claim 16 embodies the composition of claim 15 wherein said conjugate is a fusion protein between a scFv and TNF. Claim 17 embodies the method of claim 15 wherein said conjugate is recombinantly produced by fusing a gene encoding said scFv to a gene encoding TNF.

The combination of King et al and Rosenblum et al render obvious the compositions and pharmaceutical composition wherein the e23 antibody is chemically linked to TNF. The combination does not teach the recombinant fusion of TNF to e23.

Gillies et al teach the recombinant fusion of TNF-alpha to the heavy chain variable region of an antibody (column 11, lines 25-50). Gilles et al teach that the recombinant method is superior to the chemical conjugation because it avoids the unexpected consequences associated with chemical coupling (column 1, lines 42-51)

It would have been prima facie obvious at the time the claimed invention was made to fuse TNFalpha to the e23 antibody in lieu of chemical conjugation. One of skill in the art would have been motivated to do so by the teachings of Gillies regarding the avoidance of the unexpected consequences associated with chemical conjugation.

All other rejections and objections as set forth in the final office action are withdrawn.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 10-6:30 M-F.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571)272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Karen A. Canella, Ph.D.

6/12/2006

  
KAREN A. CANELLA PH.D.  
PRIMARY EXAMINER